Application Serial No.: 09/940,686

Filed: August 27, 2001

Page 3

PATENT Attorney Docket No.: UCSD1320-1

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

- 1. (currently amended) A method for achieving an optimal function of a biochemical reaction network in a cell comprising:
- (a) using optimization-methods to calculate the <u>calculating</u> optimal properties of a biochemical reaction network <u>by applying a computational optimization method to a list of reactions representing said biochemical reaction network;</u>
- (b) altering <u>said list a listing</u> of reactions in the biochemical reaction network and re-computing the optimal properties;
 - (c) repeating b) until [[the]] a desired optimal function is reached;
- (d) constructing the genetic makeup of a cell to contain the biochemical reactions which result from (c);
- (e) placing the cell constructed under (d) in culture under a specified environment to obtain a population of cells; and
- (f) cultivating the cells as in step (e) for a sufficient period of time and under conditions to allow the cells to evolve to the desired optimal function determined under (c), wherein the biochemical reaction network comprises a comprehensive biochemical reaction network.
- 2. (original) The method of claim 1, wherein the biochemical network is a metabolic network.
- 3. (withdrawn) The method of claim 1, wherein the biochemical network is a regulatory network.

Application Serial No.: 09/940,686

Filed: August 27, 2001

Page 4

4. (original) The method of claim 1, wherein the cells are prokaryotic cells.

PATENT

Attorney Docket No.: UCSD1320-1

- 5. (withdrawn) The method of claim 1, wherein the cells are eukaryotic cells.
- 6. (withdrawn) The method of claim 5, wherein the eukaryotic cells are fungal cells, animal cells, or cell lines.
- 7. (original) The method of claim 1, wherein step (d) comprises altering one or more genes in the cell.
- 8. (original) The method of claim 7, wherein altering comprises introduction of a gene or genes into the cell.
- 9. (original) The method of claim 7, wherein altering comprises modification of an endogenous gene or genes in the cell.
- 10. (original) The method of claim 1, wherein the biochemical reaction network comprises a substantially whole biochemical reaction network.
- 11. (withdrawn) An enriched population of cells produced by the method of claim 1.
- 12. (withdrawn) An enriched biomolecule produced by the method of claim 1.
- 13. (withdrawn) A method of constructing optimal functions of a substantially whole biochemical reaction network in a cell comprising:

Application Serial No.: 09/940,686

Filed: August 27, 2001

Page 5

(a) providing a database including biochemical reactions in the network;

(b) using optimization methods to calculate the optimal properties of the network;

PATENT

Attorney Docket No.: UCSD1320-1

- (c) receiving a user's selection for altering the reactions in the network and recomputing the optimal properties;
 - (d) repeating optimization until the desired property criterion is met;
- (e) displaying the results of the optimization for constructing the genetic makeup of a cell so that it contains the biochemical reactions as result of the optimization information;
- (f) culturing the cells constructed under the specified environment conditions; and
- (g) cultivating the cells for a sufficient period of time so that the cells evolve to the desired optimal performance.
- 14. (withdrawn) A computer system comprising:
 a database including biochemical reaction networks of at least one organism; and

a user interface capable of receiving a selection of two or more of said biochemical reaction networks for comparison and optimization of at least one biochemical reaction network.

- 15. (withdrawn) The system of claim 14, wherein the database is an internal database.
- 16. (withdrawn) The system of claim 14, wherein the database is an external database.
- 17. (withdrawn) The computer system of claim 14, wherein the genetic sequences are selected from ESTs, full-length sequences, or combinations thereof.

Application Serial No.: 09/940,686

Filed: August 27, 2001

Page 6

18. (withdrawn) The computer system of claim 14, wherein the sequences include amino acid sequences.

PATENT

Attorney Docket No.: UCSD1320-1

- 19. (withdrawn) The computer system of claim 14, wherein the user interface further comprises links which a user may select to access additional information relating to said biochemical reaction network.
- 20. (withdrawn) A computer program product comprising a computer-usable medium having computer-readable program code embodied thereon relating to a database including biochemical reaction networks of one or more organisms, said networks encoded by multiple genomic sequences, at least some of which represent open reading frames located along one or more contiguous sequences on each the one or more organisms' genomes, the computer program product comprising computer-readable program code for effecting the following steps within a computing system:

providing an interface for receiving a selection of desired optimal properties of said networks;

determining optimal properties of said network; and displaying the results of said determination.

- 21. (withdrawn) A method for achieving a desired optimal function of a comprehensive biochemical reaction network in a living cell comprising:
- (a) representing a listing of the biochemical reactions in the network in a computer;
- (b) using optimization methods to calculate the optimal properties of the network;
- (c) altering the list of reactions in the network and re-computing the optimal properties; and
 - (d) repeating c) until the desired optimal function is reached.

Application Serial No.: 09/940,686

Filed: August 27, 2001

Page 7

PATENT Attorney Docket No.: UCSD1320-1

- 22. (withdrawn) The method of claim 21, further comprising:
- (e) constructing the genetic makeup of a cell to contain the biochemical reactions which result from (d);
- (f) placing the cells constructed under (e) in culture under a specified environment; and
- (g) cultivating the cells as in step (f) for a sufficient period of time and under conditions to allow the cells to evolve to the desired optimal function determined under (d).